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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/494,282 01/18/00 SELIFONOV

S 02-028930US

022798 HM12/0309
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EXAMINER

ZHOU, S ART UNIT	PAPER NUMBER
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14

1631
DATE MAILED:

03/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/494,282

Applicant(s)

SELIFONOV ET AL.

Examiner

Shubo "Joe" Zhou

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2001 and 22 January 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 January 2000 is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

DETAILED ACTION

Applicants' Election/Amendment of Group II (claims 43-53) without traverse and canceling of claims 1-42 and 54-88, in Paper No. 11, filed 01/12/01, as well as the amendment in Paper No. 13, filed 1/22/01, is acknowledged and entered. Accordingly, only claims 43-53 are pending in the instant application.

Specification

The specification is objected to because of the following:

The abstract has multiple titles, which makes the abstract be composed of more than one paragraphs. See MPEP section 608.01(b).

The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at page 8 and elsewhere. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01.

See also the enclosed Notice of Draftsperson's Patent Drawing Review.

Appropriate correction is required.

Claim Rejections-35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-53 are rejected under 35 U.S.C. 112 , second paragraph, as being vague, indefinite and confusing for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 43 and all its dependent claims is "a method of making character strings", but it is not clear from the steps of the method what character strings are made. Is "a set of derivatives of the parental character strings" the character strings meant in the preamble?

The phrase "the method of claim 48" in claims 50-53 are confusing since claim 48 claims a library, not a method.

Claim Rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 43-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. (IDS document: Nature Biotechnology, Vol. 16:258-261, March, 1998).

Zhao et al. disclose a procedure for molecular evolution by staggered extension process *in vitro* recombination comprising providing a plurality of parental nucleic acids, RC 1 and RC 2, which nucleic acids comprises 10 differences as listed in Table 1 (see page 258 and 259). Given the broad meanings of the phrase "character string" and the word "oligonucleotide", all the nucleic acids disclosed by Zhao et al. and those that are synthesized during the process of staggered extension, are interpreted as character strings, and all the nucleic acids that are less than the full-length of the RC 1 and RC 2 genes are interpreted as "oligonucleotides". Thus, Zhao et al. provide two parental character strings "encoding thermostable B. subtilis subtilisin E variants, each of which carries a single thermostable mutation along with several other neutral mutations" (see page 258, right column), provide a set of oligonucleotide character strings of preselected length that encode a plurality of single-stranded oligonucleotide subsequences (see page 261), and create a set of derivatives of the parental character strings, which character strings comprise sequence variant strings each having at least one mutations, the set having a plurality of mutations.

Given the nature of Zhao et al.'s methodology, a PCR procedure to produce recombinants *in vitro*, it is obvious that at different cycles of the procedure as shown in Figure 1, the "oligonucleotides" in the reactions are different in length and sequences, and they overlap each others, as required in the instant claim 44, e.g. the oligonucleotides shown in steps B and C of Figure 1, wherein the oligonucleotides in C overlap those in B. Zhao et al. disclose 10 positions in the parental genes including thermostable mutations and neutral mutations and use the positions to define segments along the genes and expect recombination/crossover between the positions, therefore,

at least one genetic operator, a mutation and/or a crossover is applied (as required in the instant claim 45). During the procedure of Zhao et al.'s staggered extension, at a particular cycle after several cycles as shown in Figure 1, B and C in page 259, a set of overlapping character strings, i.e. the two parental nucleic acids, is provided, and sets of single-stranded oligonucleotides, e.g. those in Figure 1, B and C, are synthesized, as required in the instant claim 46. In addition to the procedure of staggered extension, Zhao et al. also disclose and compare other in vitro recombination methods including assembly PCR and error-prone assembly PCR and recombinant nucleic acids are selected for improved activity and provided (see page 260, right column), and obviously a library is assembled by assembly PCR from the single-stranded oligonucleotides before the recombinants are selected, as required in the instant claims 47-49. At least 10 recombinants are selected and sequenced, and around 368 clones from the library are selected and characterized, as required in the instant claims 50-53.

Conclusion

No claim is allowed.

Enclosed please find *inter alia* a copy of the PTO-1449 forms with multiple references lined through because the references do not have a publication date. Although these references will not be listed on PTO-1449, they have been considered by the Examiner.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG

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61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)).
The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:

Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is 703-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

S. "Joe" Zhou: sjz 
Patent Examiner
March 6, 2001


ARDIN H. MARSCHEL
PRIMARY EXAMINER

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities--37 CFR 1.85

File new drawings with the changes incorporated therein. The application number or the title of the invention, inventor's name, docket number (if any), and the name and telephone number of a person to call if the Office is unable to match the drawings to the proper application, should be placed on the back of each sheet of drawings in accordance with 37 CFR 1.84(c). Applicant may delay filing of the new drawings until receipt of the Notice of Allowability (PTOL-37). Extensions of time may be obtained under the provisions of 37 CFR 1.136. The drawing should be filed as a separate paper with a transmittal letter addressed to the Drawing Processing Branch.

2. Timing for Corrections

Applicant is required to submit **acceptable** corrected drawings within the three-month shortened statutory period set in the Notice of Allowability (PTOL-37). If a correction is determined to be unacceptable by the Office, applicant must arrange to have acceptable corrections resubmitted within the original three-month period to avoid the necessity of obtaining an extension of time and paying the extension fee. Therefore, applicant should file corrected drawings as soon as possible.

Failure to take corrective action within set (or extended) period will result in **ABANDONMENT** of the Application.

3. Corrections other than Informalities Noted by the Drawing Review Branch on the Form PTO-948

All changes to the drawings, other than informalities noted by the Drawing Review Branch, **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.